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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,222	01/15/2002	Ping Gao	C-3407/1/US	5749

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	**PAPER NUMBER**
1615	8

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,222	GAO ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-92 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-92 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claims 19 – 93 are objected to because of the following informalities: claims 19 – 48 are misnumbered, the claims should be numbered one less than indicated by the claim number; claims 50 – 93 are misnumbered, the claims should be numbered two less than indicated by the claims number. Also the dependent claims must be renumbered accordingly. Appropriate correction is required.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 2, 4 – 16, 21 – 28, 31 – 38, 41 – 46, 50 – 52, 56 – 59, 62, 63, 66 – 80, and 86 – 93 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 – 12, 18 – 20, 24 – 32 of copending Application No. 10/119,118. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to an orally deliverable pharmaceutical composition comprising a cyclooxygenase-2-inhibitor, a solvent

liquid, turbidity-decreasing polymer, a vasomodulator and/or an alkylxanthine compound. The turbidity-decreasing polymers are identical to those of the instant application. The cyclooxygenase-2-inhibitor, liquid solvents and other active ingredients are identical to those of the instant application. The difference in the set of claims is that the claims of the co-pending application further comprise a free-radical scavenging antioxidant, yet the claims of the instant application comprise open claim language, which allows for the inclusion of the free-radical scavenging antioxidants. One of ordinary skill in the art would be motivated to interchange the invention of the co-pending application with those of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 1-3, 6-12, 14-16, 28, 31-33, 37 – 39, 42 – 48, 51, 52, 66 – 68, 72 – 75, 78 –80, 86 and 87 are rejected under 35 U.S.C. 102(a) as being anticipated by Gao et al (WO 00/32189). The claims are drawn to an oral formulation comprising a COX-2 inhibitor of low water solubility, a solvent liquid and a turbidity-decreasing polymer. Celecoxib is recited the COX-2 inhibitor, polyvinylpyrrolidone and cellulosic polymers are recited as possible turbidity-decreasing polymers, and polyethylene glycol is listed as the solvent.

Gao et al discloses a celecoxib capsule formulation comprising common carriers and excipients known in the art. Polyvinylpyrrolidone, and hydroxypropylmethylcellulose are listed as carriers (page 21, lines 30 – 33), and polyethylene glycol is listed as a solvent (page 23, line 10). The composition comprises one or more unit dosages of celecoxib comprising 50 mg to about 400 mg of the drug (page 15, line 16 – 18). The reference also discloses a method of treating a patient in need of analgesia with doses of the celecoxib formulation (page 8, line 23 – page 13, line 3). These disclosures along with others render the claims anticipated.

5. Claims 1,2, 7 – 10, 14 – 16, 27, 28, 31 – 38, 42 – 46, 51, 52, 62, 63, 66 – 72, 75, 77 – 80, 86 and 87 are rejected under 35 U.S.C. 102(a) as being anticipated by Tanida et al (USPN 6,214,378). The claims are drawn to an oral formulation comprising a COX-2 inhibitor of low water solubility, a solvent liquid and a turbidity-decreasing polymer. Celecoxib is recited the COX-2 inhibitor, polyvinylpyrrolidone and cellulosic polymers are recited as possible turbidity-decreasing polymers, and polyethylene glycol is listed as the solvent with a molecular weight between 375 to about 400.

Tanida et al discloses capsules comprising hydroxypropylmethylcellulose, polyvinylpyrrolidone, polyethylene glycol and COX-2 inhibitors, specifically celecoxib (col. 3, lin. 40 – 57; col. 4, lin. 15 – 17; examples). Also disclosed by the reference are imbibable liquid formulations (examples). These disclosures render the claims anticipated.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 2, 6 – 10, 14 – 16, 27, 28, 31 – 38, 42 – 46, 51, 52, 62, 63, 66 – 72, 75, 77 – 80, 86 and 87 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*). The claims are drawn to an oral formulation comprising a COX-2 inhibitor of low water solubility, a solvent liquid and a turbidity-decreasing polymer. Celecoxib is recited the COX-2 inhibitor, polyvinylpyrrolidone and cellulosic polymers are recited as possible turbidity-decreasing polymers, and polyethylene glycol is listed as the solvent with a molecular weight between 375 to about 400.

Tanida et al discloses capsules comprising hydroxypropylmethylcellulose, polyvinylpyrrolidone, polyethylene glycol and COX-2 inhibitors, specifically celecoxib (col. 3, lin. 40 – 57; col. 4, lin. 15 – 17; examples). Also disclosed by the reference are imbibable liquid formulations (examples). These disclosures render the claims anticipated.

7. Claims 1, 2, 6, 14 – 16, 21 – 24, 27, 28, 31, 32, 36 – 38, 42, 51, 52, 56 – 59, 62, 63, 66, 67, 71 – 73, 77 – 80, 86 – 93 are rejected under 35 U.S.C. 102(b) as being anticipated by Black et al (USPN 5,733,909). The claims are drawn to an oral formulation comprising a COX-2 inhibitor of low water solubility, a solvent liquid and a turbidity-decreasing polymer. The composition further comprises an alkylxanthine compound such as caffeine.

Black et al discloses a capsule formulation comprising COX-2 inhibitors or pharmaceutical salts thereof combined with other active agents such as caffeine and theobromine (col. 7, lin. 52 – col. 8, lin. 60). The formulation comprises liquid PEG, along with hydroxypropylmethylcellulose (col. 10, lin. 30 – 43). Syrup and elixir formulations are also

disclosed (col. 11, lin. 19 – 25). A method of treating a patient in need is also disclosed by the reference (col. 11, lin. 7 – col. 12, lin. 38). These disclosures along with others render the claims anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 4, 5, 17 – 20, 25, 26, 40, 41, 53 – 55, 60, 61, and 81 – 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao et al (WO 00/32189) in view of Hanna et al (USPN 4,601,894). The claims are drawn to a celecoxib composition is recited the COX-2 inhibitor, polyvinylpyrrolidone and cellulosic polymers are recited as possible turbidity-decreasing polymers, and polyethylene glycol is listed as the solvent. For the cellulosic polymer

hydroxypropylmethylcellulose is the preferred excipient. The polymer has about 15% to about 35% methoxyl substitutions and about 3% to about 15% hydroxypropoxyl substitution.

As discussed above Gao discloses a celecoxib formulation comprising hydroxypropylmethylcellulose. What is lacking in the reference is a disclosure of the particular methoxyl and hydroxypropoxyl substitution concentrations. Hanna et al discloses a formulation comprising a hydroxypropylmethylcellulose with about 19% to about 24% methoxyl substitution and about 7% to about 12% hydroxypropoxyl substitution (col. 2, lin. 43 – 61). The formulation comprises the analgesics acetaminophen and can be formulated into capsules (col. 1, lin. 60 – 63). It would have been obvious to one of ordinary skill in the art to combine the hydroxypropylmethylcellulose of Hanna with the formulation of Gao.

Also with regard to claims 4, 5, 25, 26, 40, 41, 60, and 61 which are drawn to the amount of COX-2 inhibitor or turbidity-decreasing polymers are dissolved into the solvent liquid, it is the position of the examiner that such limitations hold little patentable weight view of the prior art. The prior art discloses a composition where the components are dissolved into a solvent liquid and through routine experimentation, the optimum amount can be determined that would yield the best results for delivery of the active agents. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges

is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

With these things in mind a skilled artisan would have been motivated to combine the HPMC of Hanna into the formulation of Gao in order to provide a stable environment to deliver the COX-2 inhibitor. A skilled artisan would have been motivated to modify the concentrations disclosed by Gao in order to optimize the release and delivery of the celecoxib formulation. It would have been obvious to a skilled artisan at the time of the invention to combine and modify the teachings of the art with an expected result of a stable capsule formulation of celecoxib useful in treating various disorders.

9. Claims 13 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*) or Gao et al (WO 00/32189) in view of Guess et al (USPN 6,054,455). The claims are drawn tot a composition where the active agent is valdecoxib.

As discussed above Tanida and Gao disclose celecoxib formulations. Valdecoxib is a well-known COX-2 inhibitor, which can be used in place of or in conjunction with celecoxib. This is seen in Guess, which discloses capsule formulations possibly comprising celecoxib, valdecoxib and other COX-2 inhibitors, in capsule form (col. 32, lin. 27 – 29; col. 33, lin. 18 – 21). Since the compounds are so well known and studied it would be well within the level of skill in the art to substitute the valdecoxib of Guess into the formulation of either Tanida or Gao.

With this in mind a skilled artisan would have been motivated to substitute the valdecoxib of Guess into the formulations of either Tanida or Gao in order to treat a wider

variety of disorders and ailments. It would have been obvious to a skilled artisan at the time of the invention to make the substitution with an expected result of a COX-2 capsule formulation capable of treating a variety of disorders.

10. Claims 29, 30, 64, 65, 84 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation of the Japanese document*). The claims are drawn to a capsule comprising celecoxib, and a cellulosic polymer dissolved into the wall of the capsule.

As discussed above the Tanida et al discloses a capsule formulation comprising celecoxib and HPMC (col. 2, lin. 54 – col. 3, lin. 41). The HPMC acts as the base for the capsule, yet the reference does not disclose a percentage to which the polymer is present in the capsule wall. However this determination can be made through routine experimentation and optimization of ranges, all of which is well within the limits of one of ordinary skill in the art.

With his in mind a skilled artisan would have been motivated to follow the suggestions and teachings of Tanida in order to optimize the amount of turbidity-decreasing polymer in the wall of the capsule in order to optimize the stability and release of the COX-2 inhibitor. It would have been obvious to one of ordinary skill in the art to follow the suggestion of the art in this way with an expected result of a COX-2 inhibitor capsule formulation with improved solubility and quicker release.

11. Claim 76 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tanida et al (WO 98/05310; *the citations will refer to the English equivalent USPN 6,214,378 pending translation*

of the Japanese document) in view of Kawata et al (USPN 4,343,789). The claim is drawn to a composition comprising a drug of low water solubility in a high-energy state, in capsule form where the capsule wall comprises a cellulosic polymer.

As discussed above Tanida discloses a capsule formulation where the active agent is in a high-energy state (salt thereof), where the wall of the capsule comprises a cellulosic polymer. What is lacking in the reference is a disclosure of the active agents in an amorphous form. The drugs are present in their salt forms however. Kawata discloses amorphous forms of indomethacin (abstract; col. 2, lin. 39 – 44). Tanida discloses a high-energy state of indomethacin as well. It would have been obvious to include the amorphous form of Kawata into the capsule formulation of Tanida.

One of ordinary skill in the art would have been motivated to combine the high-energy amorphous form of indomethacin into the capsule formulation of Tanida in order to improve the solubility of the drug and provide a faster release to the active agent. It would have been obvious to skilled artisan to combine the teachings as such, with an expected result of a capsule formulation capable of treating various disorders quickly.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

MP Young

THURMAN K. PAGE
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